

Fig. 1A-1

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```

835      845      855      865      875      885      895
GGCACAGCCTGGGCCCTGCTCTGAGTATGACAGAGAGCCCCCTGGGAAGTTGTAGTGGAGGAAAGACAGGTTCATGA
  910      920      930      940      950      960      970
CTAGGAAAAAGCAATCCCTCTGTGTGGGTGGAAGGAGTTGCAGTGTGTGTGAGAGAGAGACAAGACAGAC
  985      995     1005     1015     1025     1035     1045
AGACAGACACTTCTCAATGTTTACAAGTGTCTCAGGCCCTGACCCGGAATGCTTCCAAATTACGTTAGTCTCTGGAAA
      EcoO      BsmI+      SnaBI
1060     1070     1080     1090     1100     1110     1120
ACCCCCGTGATCATTTTCACTACTCAAGAAACCTCGGGAGTGTCTTCTCTGAAGGTCATCAGGTTTGTGACTC
  1135     1145     1155     1165     1175     1185     1195
TCTGCTGTCTCATTTCTTCTGTGTGTGTGATGGTTGTCTGCCAGGCCCTGTCCCGCATCCTCTCTTGCCC
      EcoO
1210     1220     1230     1240     1250     1260     1270
CTGCAGAGGGATGAGTGTGTGGGGCCCTCACGAGTTGAGTTGTTCATAAGCAGAGATCTCTTTGAGCAGGGCGCCT
PstI      EcoO      BglII      NarI PS
1285     1295     1305     1315     1325     1335     1345
GCAGTGGCCTTGTGTGAGGCTGGAGGGGTTTCGATTCCCTTATGGAATCCAGGCAGATGTAGCATTTAAACAACA
tI
1360     1370     1380     1390     1400     1410     1420
CACGTGTATAAAAGAAACCAGTGTCCGCAGAAAGTTCCAGAAAGTATTATGGGATAAGACTACATGAGAGAGGAA
  1435     1445     1455     1465     1475     1485     1495
TGGGGCATTTGGCACCTCCCTTAGTAGGGCCTTTGCTGGGGTAGAAATGAGTTTAAAGGCAGGTTAGACCCCTCGA
      EcoO      BspMI-
1510     1520     1530     1540     1550     1560     1570
ACTGGCTTTTGAATCGGGAATTTACCCCCAGCCGTTCTGTGCTTCAATTGCTGTTCACATCAGTGCCTAAGATG
  1585     1595     1605     1615     1625     1635     1645
GAGGAACCTTTGATGTGTGTGTCTTTCTCCTCACCTGGGCTCTGCTTCTTCACTTCTTGTCAATGCAGAGAA
  1660     1670     1680     1690     1700     1710     1720
CAGCAGCAGGCCACAGAGCGGCCCTTGTAAAGAACGACGAGCTGTATGTTCAGCTTCCGAGACCTGGGCTGGCAGG
      StuI      BspMI
1735     1745     1755     1765     1775     1785     1795
TAAGGGGCTGGCTGGGTCTGTCTTGGGTGTGGGCCCTCTTGGCGTGGGCTCCACAGGCAGCGGGTGTGTGCTCA
      ApaI      EcoO

```

Fig. 1A-2

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1810 1820 1830 1840 1850 1860 1870
 GTCTGTTTCTCATCTCTGCCAGTTAAGACTCCAGTATCAAGTGGCCTCGCTAGGGAAGGGTACTTGGCTAAGGA
 1885 1895 1905 1915 1925 1935 1945
 TACAGG.....(APPROX. 1000 BASES).....GGGAGCCAGCATGGGTGATGCCATTATGA
 1960 1970 1980 1990 2000 2010 2020
 GTTATTAGCCTCTCTGGCAGGTGGGCAACCGAGGCATGGAGGTTGTGTTAAGGTGAACCTGCCAGTGTGTGACCA
 BglI BspMI- Dr
 2035 2045 2055 2065 2075 2085 2095
 CCTAGTGGGTAGAGCTGATGATTGCCTCACACCGGAGCTCCTTCTGTGCGCGTCTGTCTCCAGAAACACAGC
 aIII Pfl
 MI SacI N
 2110 2120 2130 2140 2150 2160 2170
 CATGGATGTCCATTTTAGGATCAGCCAGCCCGCTCTGTGCTTCATTTTATTTATTTTATGTTTATTAGAAATGGG
 coi
 2185 2195 2205 2215 2225 2235 2245
 GTCTTGCTCTGTACCCAGGCTGGGTGCAGTGGTGTGATCATAGCTCACCGCAGCTTTGACGCGCTCTTCCCCT
 TthlII
 2260 2270 2280 2290 2300 2310 2320
 CAGTCTACTAAGCTTGACTATAGGCCAAGACTATAGAGTGTCTCTTCCATTCTTTTGGACCATGAGAGG
 HindIII BstXI
 2335 2345 2355 2365 2375 2385 2395
 CCACCCATGTTTCCCTGCTGGGCTGCTGCTCAGAAAGGCATGGTCTGAGGCTTTTCACCTTGGTCGTGAG
 ApaI
 EcoO
 2410 2420 2430 2440 2450 2460 2470
 CCTTCGTGGTGGTTTCTTTCAGCATGGGTTGGATGCTGTGCTCAGGCTTCTGCATGTTTCCACACTCTCTT
 2485 2495 2505 2515 2525 2535 2545
 CTCCTCCTCAGGACTGGATCATCGCGCTGAAGGCTACGCGCGCTACTACTGTGAGGGGAGTGTGCCCTTCCCTC
 MstII BssHI
 2560 2570 2580 2590 2600 2610 2620
 TGAACCTCCTACATGAACGCCACCAACCGCCATCGTGCAGACGCTGTGGGTGTACGCCCATCTTGGGGTGTGG
 BS
 2635 2645 2655 2665 2675 2685 2695
 TCACCTGGCGGCGAGGCTGGGGGCCACACAGATCCTGCTGCCCTCCAAGCTGGGGCCTGAGTAGATGTCAGCCC
 tEI BglI EcoO

Fig. 1A-3

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2710 2720 2730 2740 2750 2760 2770
ATTGCCATGTCATGACTTTTGGGGGCCCTTGGCCGTTAAATAAAATCAAAAATTGTACTTTATGACTGGTTT
ApaI
2785 2795 2805 2815 2825 2835 2845
GGTATAAGAGGAGTATAATCTTCGACCCTGGAGTTCATTATTCTCTAAATTTTAAAGTAACATAAAAGTTGT
DraI
2860 2870 2880 2890 2900 2910 2920
ATGGGCTCCTTTGAGGATGCTTGTAGTATTGTGGGTGCTGGTTACGGTGCCTAAGAGCACTGGGGCCCTGCTTCA
ApaI
2935 2945 2955 2965 2975 2985 2995
TTTTCCAGTAGAGGAAACAGGTAAACAGATGAGAAATTTTCAGTGAGGGGCACAGTGATCAGAAGCGGGCCAGCAG
3010 3020 3030 3040 3050 3060 3070
GATAATGGGATGGAGAGATGAGTGGGGACCCATGGGCCATTTCAAGTTAAATTTTCAGTCGGGTCAACCAAGGAAGAT
BstEII
3085 3095 3105 3115 3125 3135 3145
TCCATGTGATAATGAGATTACGTGCCAGTCACGGGCACACTCAGTAGGTGTTATTCCTGCTCTGCCAACAGCA
3160 3170 3180 3190 3200 3210 3220
ACCATAGTTGATAAGAGCTGTTAGGGATTTTGTCTCTTTGCTTAGAATCCAAGGTTCAAGGACCTTGGTTATGTA
EcoO
3235 3245 3255 3265 3275 3285 3295
GCTCCCTGTCATGAACATCATCTGAGCCCTTTCCTGCCCTACTGATCATCCACCCTGCCCTTGAATGCTTCTAGTGAC
BsmI+
3310 3320 3330 3340 3350 3360 3370
AGAGAGCTCACTACCAGGACTACTCCCTCCTTTCATTAGTAATCTGCCCTCCTTCTTTCTTGTCCCTGTCTGT
SacI
3385 3395 3405 3415 3425 3435 3445
GTGTTAAGTCCTGGAGAAAAATCTCATCTATCCCTTTTCATTGATTTCTGCTCTTTGAGGGCAGGGGTTTTTGT
3460 3470 3480 3490 3500 3510 3520
CTTTGTTGTTTTTTAAGTGTGGTTTTCCAAAGCCCTTGCTCCCTCCTCAATTGAAACTTCAAAGCCCTCAT
3535 3545 3555 3565 3575 3585 3595
TGGGATTGAAGGTCCTTAGGCTGGAAACAGAGAGTCCTCCCAACCTGTTCCCTGGCCTGGATGTGCTGTGCTG
EcoOmsII

Fig. 1A-4

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3610 3620 3630 3640 3650 3660 3670
 TGCCAGTATCCCCTGGAAGTGCCAGGCATGTCTCCCGGCTGCCAGGGGACACATCTCTATCCTTCTCACAACCC
 3685 3695 3705 3715 3725 3735 3745
 CTGCGCTTCATGGCCCATGGAACAGGAGTGCCCATGCGCCCTGTGTGCACCTACTTCCATCAGTATTTCCACCAGAGAT
 BglI NcoI ApaLI BglI
 3760 3770 3780 3790 3800 3810 3820
 CTGCAGGATCAAAAGTGAATTCTCCAGGGATTGTGAAATGATGCCGATTGTGGTCATGTTTAAAGGGGCAACTGT
 I EcoRI DraI
 PstI
 3835 3845 3855 3865 3875 3885 3895
 CTTCTAGAGAGTCCTGATGAAATGCTTCCAGAGGAAATGAGCTGATGGCTGGAATTTGCTTTAAATCATTCAG
 XbaI DraI
 3910 3920 3930 3940 3950 3960 3970
 GTGGAGCAGGTGGGGAAGGTATGGATGTGTAAGAGTTTGAAATTTGCCATCATAAATGTGTAAAGCATGCT
 BspMI- SphI
 3985 3995 4005 4015 4025 4035 4045
 GGCCTATGTCAGCAGTCACAGCCCTGGAGGTGGTAACAGAGTGCCAGTCACTGATGCTCAAGCCTGGCACCTACAG
 4060 4070 4080 4090 4100 4110 4120
 TTGCTGGAAACCCAGAGTTTACCGTTGAAACACAGGACAGTGGAAATCTCTGGCCCTGTCTTTGAACACCGTGGC
 4135 4145 4155 4165 4175 4185 4195
 AGATCTGCTAACACTGATCTTGGTTGGCTGCCGTCAGCTTAGGTTGAGTGGCGGTCTTCCCTTAGTTGCTTAGT
 BglII
 4210 4220 4230 4240 4250 4260 4270
 CCCCCTATTCCCTATTGCTTACCTCGGTCTATTTTGTCTTATCAGTGGACCTCACGAGGCACTCATAGGCATTT
 4285 4295 4305 4315 4325 4335 4345
 GAGTCTATGTGTCCTGTGCCACATCCTCTGTAAAGGTGCAGAGAAGTCCATGAGCAAGATGGAGCACTTCTAGTG
 4360 4370 4380 4390 4400 4410 4420
 GGTCCAAGTCAGGGACACTATTTCAGCAATCTACAGTGCACAGGGCAGTTCCTCCCAACAGAGAATTACCTGGTCCTG
 ApaLI
 4435 4445 4455 4465 4475 4485 4495
 AATGTCGATCTGGCCCTTCTCCCTCCACTGTATAATGTGAAACCTCTATGCTTGTTCCTTGTCTGCAAA
 4510 4520 4530 4540 4550 4560 4570
 ACAGGGATAATCCCAGAACTGAGTTGTCCATGTAAAGTGCTTAGAACAGGGAGTGCTTGGCTTGGGAGTGTAC
 BS

Fig. 1A-5

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```
4585 4595 4605 4615 4625 4635 4645
CTGCAGTCATTATGCCCAGACAGGATGTTCTTTATAGAAACGTGGAGGCCAGTTAGAACGACTCACCGCT
PMI+
PstI
4660 4670 4680 4690 4700 4710 4720
TCTCACCACTGCCCATGTTTGGTGTGTGTTTCAGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCT
PflMI
4735 4745 4755 4765 4775 4785 4795
GTGCGCCACGCGAGCTCAATGCCATCTCCGTCTCTACTTCGATGACAGCTCCAACGTCAATCCTGAAGAAATACA
4810 4820 4830 4840
GAAACATGGTCCGGCCCTGTGGCTGCCACTAGCTCCTCCGA
```

Fig. 1A-6

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```

CONSENSUS PROBE      20      30      40      50      60      70
GATCCTAATGGGCTGTACGTGGACTTCCAGCGGACGTGGCTGGGACGACTGGATCATCGCCCCCGTCG
**                ** *** ***** ***** **
TGTAAGAACGACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCCTGAAG
OP4  28      38      48      58      68      78      88
80      90      100     110     120     130     140
ACTTCGACGCCCTACTACTGCTCCGGAGCCTGCCAGTTCCCTCTGCGGATCACTTCAACAGCACCAACCA
** ** ***** ** ** ***** ** *** *****
GCTACGCGCGCTACTACTGTGAGGGGAGTGTGCTTCCCTCTGAACTCCTACATGAACGCCCAACCA
98      108     118     128     138     148     158
150     160     170     180     190     200     210
CGCCGTGGTGACAGCCCTGGTGAACAACATGAACCCCGGCAAGGTACCAAGCCCTGCTGCTGCCACC
*** ***** ** ** ***** ** ***** *****
CGCCATCGTGACAGCGCTGGTCCACTTCAACAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCACG
168     178     188     198     208     218     228
220     230     240     250     260     270     280
GAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATTCCACCGTGGTGTGAAGAACTACCAGGAGA
***** ***** ** *** ***** ** ***** ***** *
CAGCTCAATGCCCATCTCCGTCTCTACTTCGATGACAGCTCCAACGTCACTCCTGAAGAAATACAGAAACA
238     248     258     268     278     288     298
290     300     310
TGACCGTGGTGGGCTGCGGCTGCCGCTAACTGCA
** ** ***** ** **
TGGTGGTCCGGGCTGTGGCTGCCACTAGCTCCT
308     318     328
```

Fig. 1B

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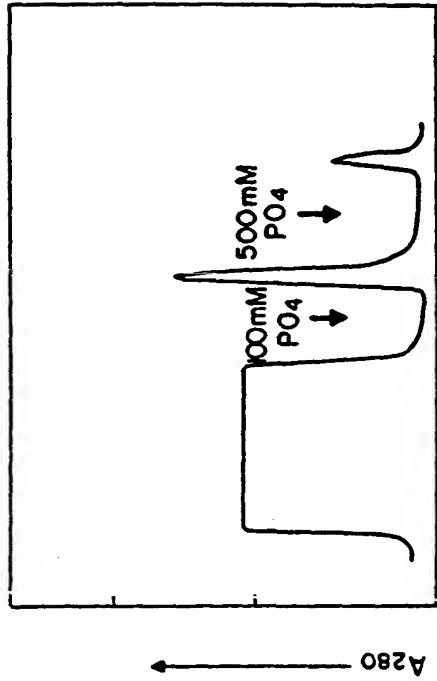
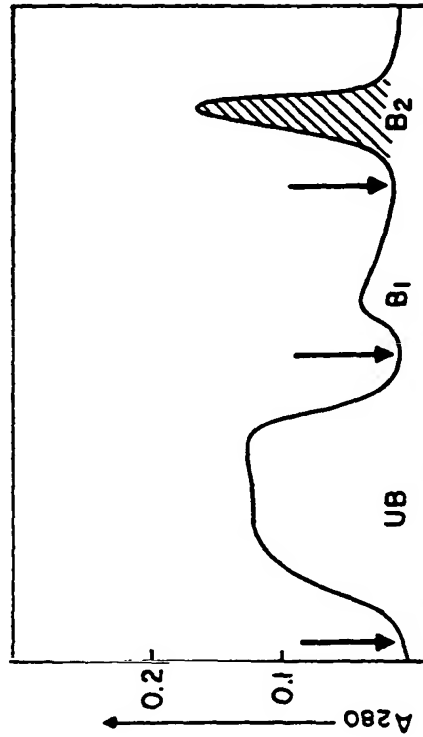


Fig. 2B



UB: 6MUREA 50mMTRIS 0.1MNaCl PH 7.0
 B1: 6MUREA 50mMTRIS 0.15MNaCl PH 7.0
 B2: 6MUREA 50mMTRIS 0.5MNaCl PH 7.0

Fig. 2D

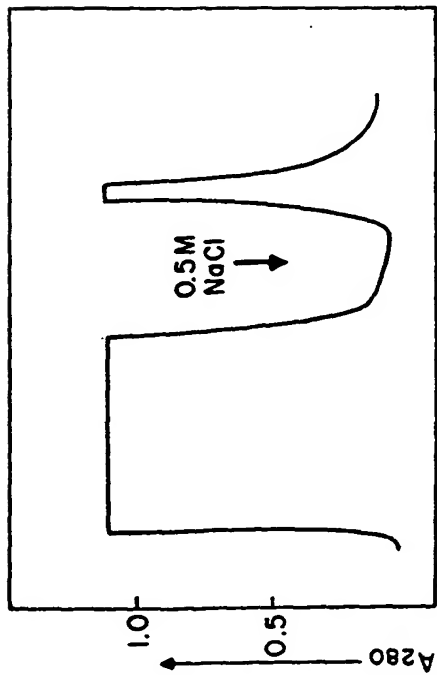
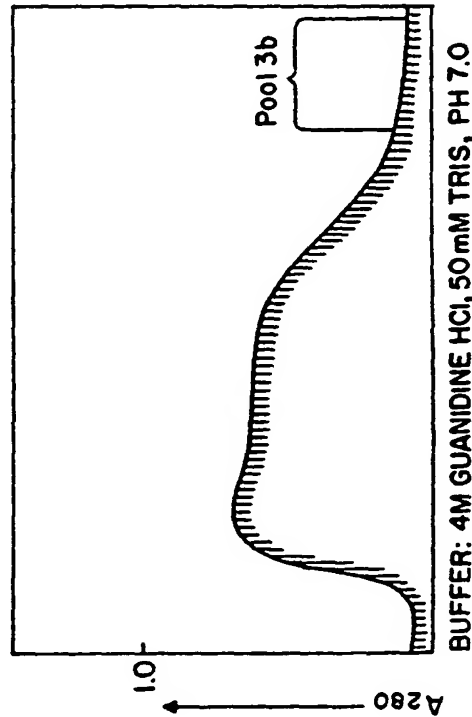


Fig. 2A



BUFFER: 4M GUANIDINE HCl, 50mM TRIS, PH 7.0

Fig. 2C

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Fig. 3A



Fig. 3B



Fig. 4A



Fig. 4B

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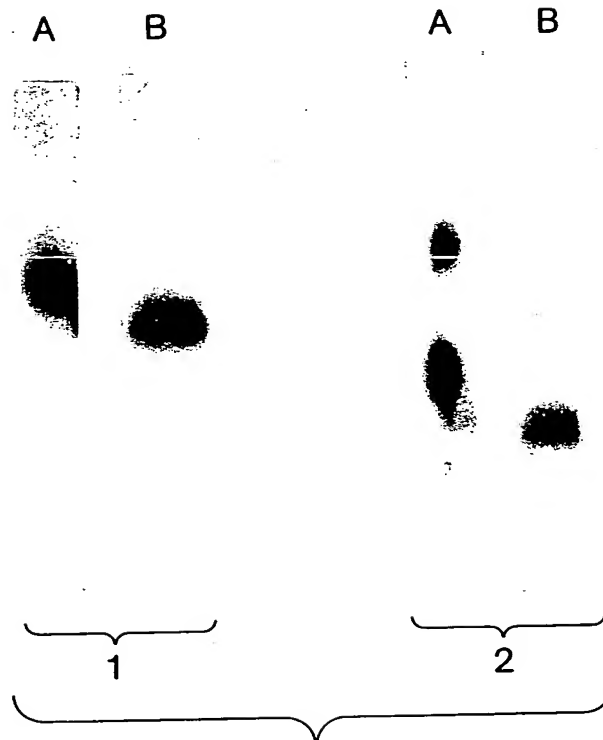


Fig. 5



Fig. 6E



Fig. 6D



Fig. 6C



Fig. 6B



Fig. 6A

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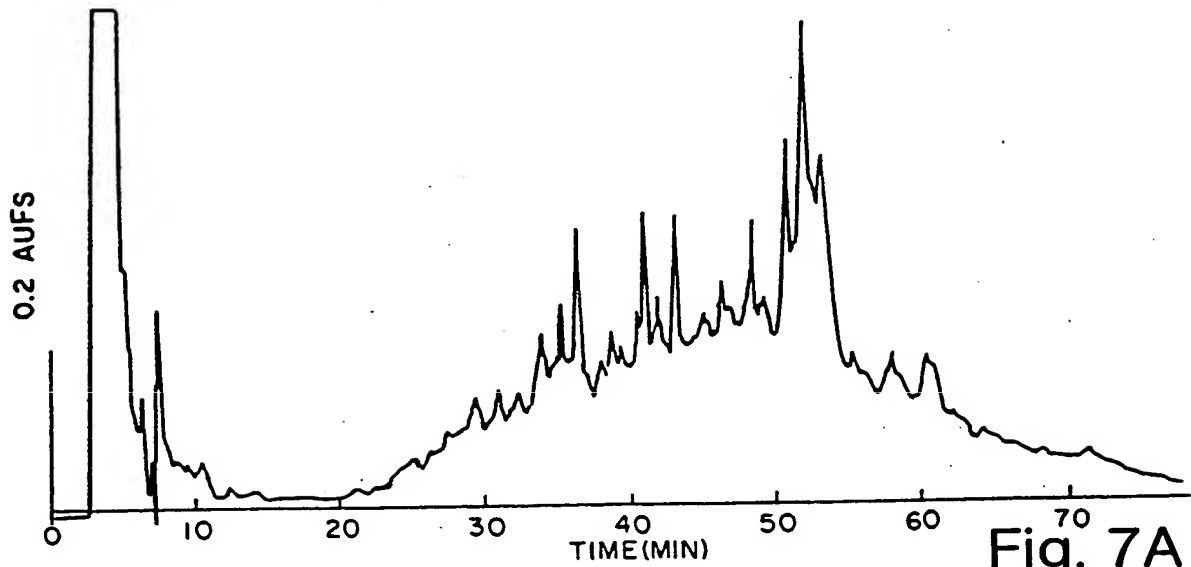


Fig. 7A

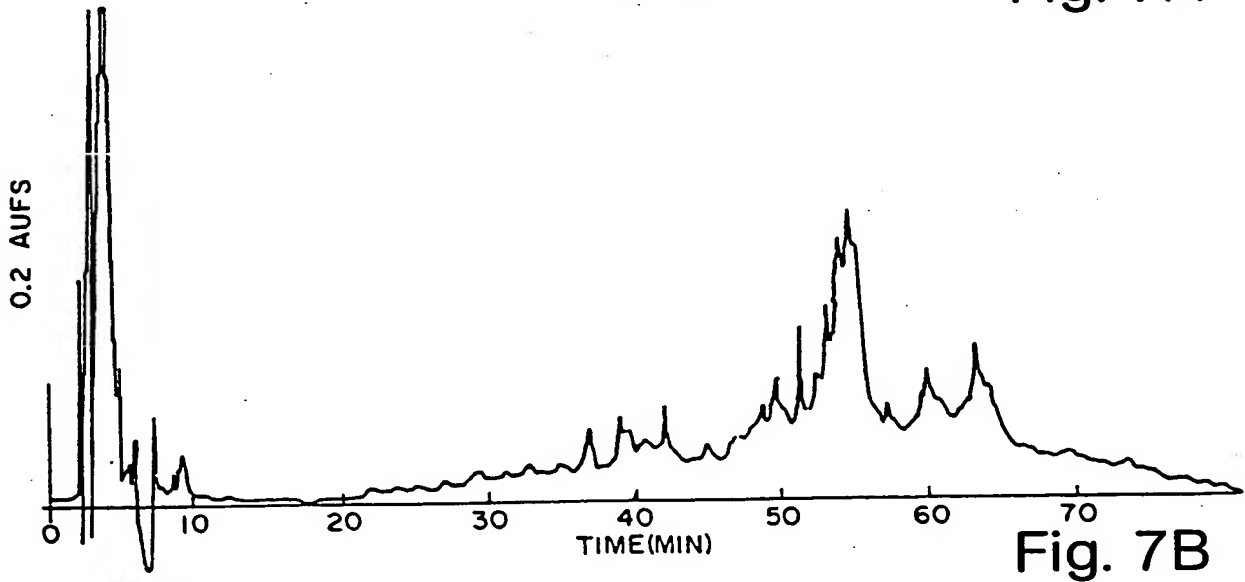


Fig. 7B

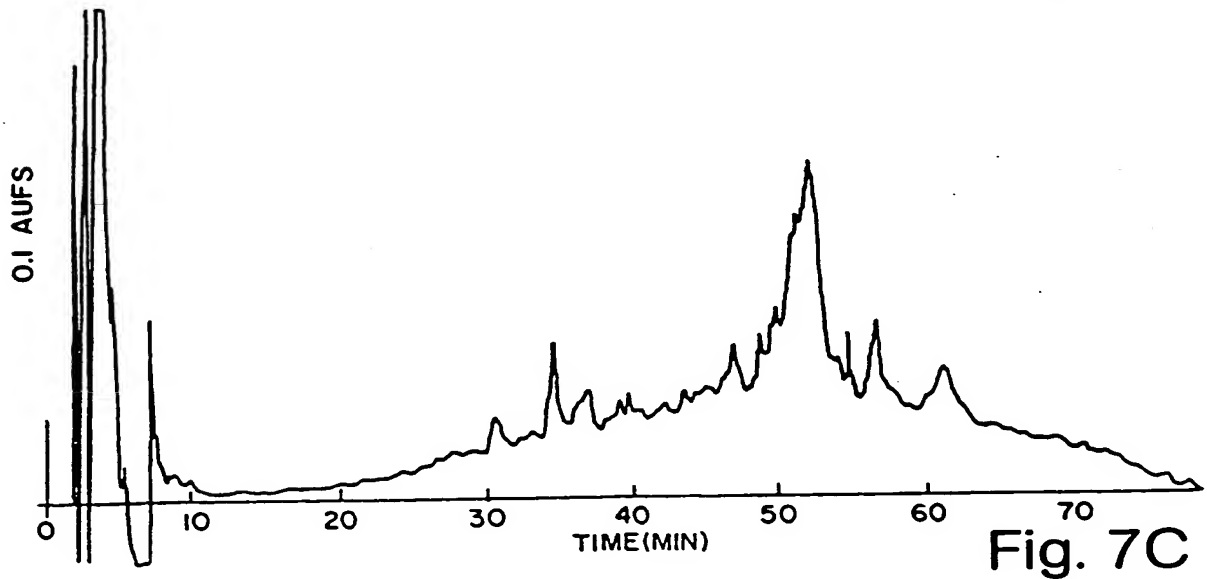


Fig. 7C

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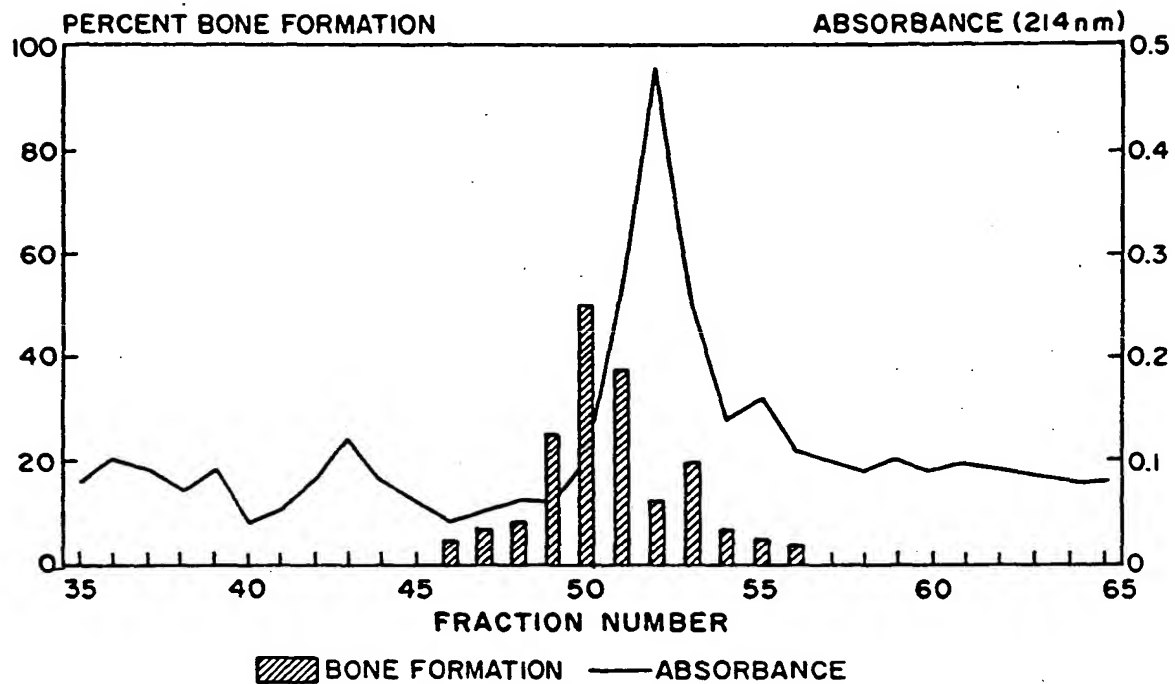


Fig. 8

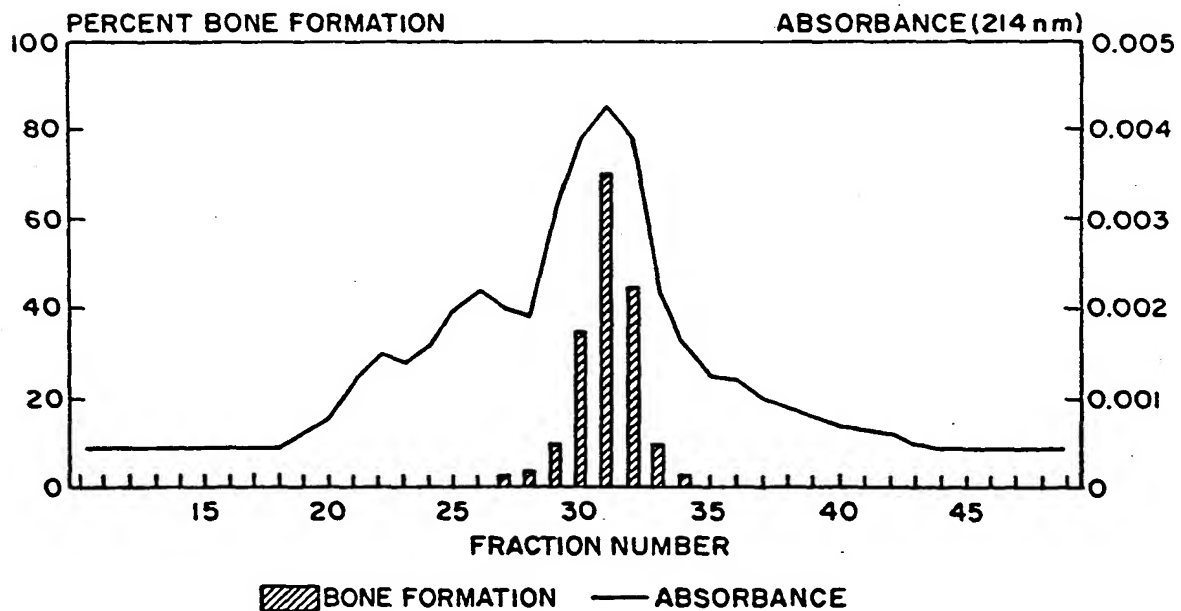


Fig. 9

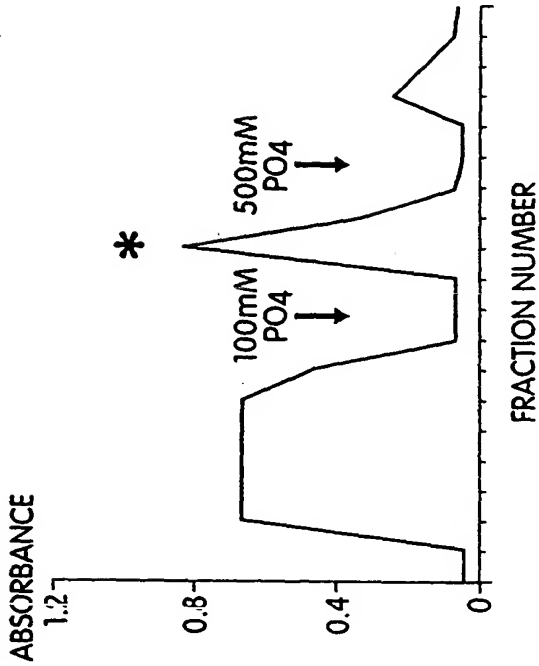


Fig. 10B

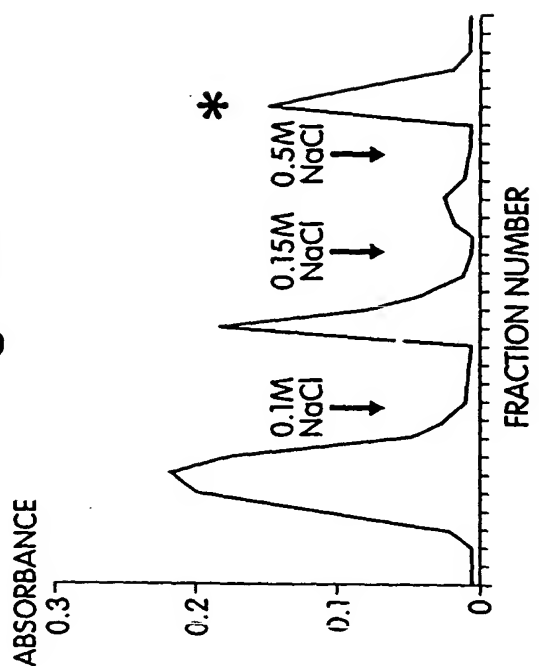


Fig. 10D

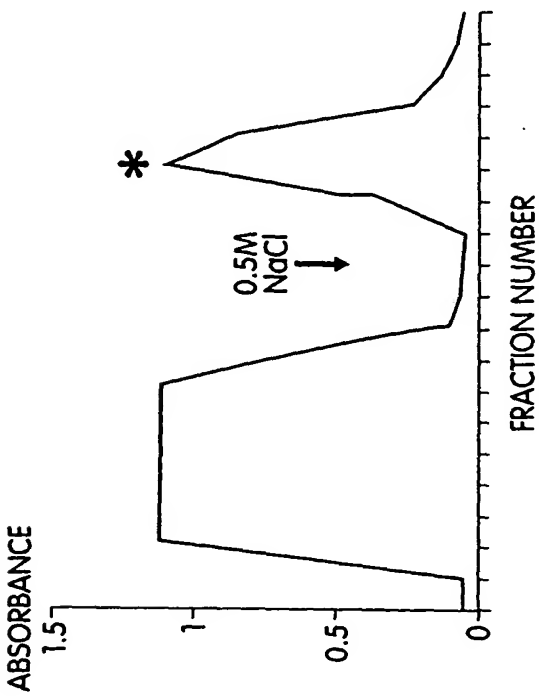


Fig. 10A

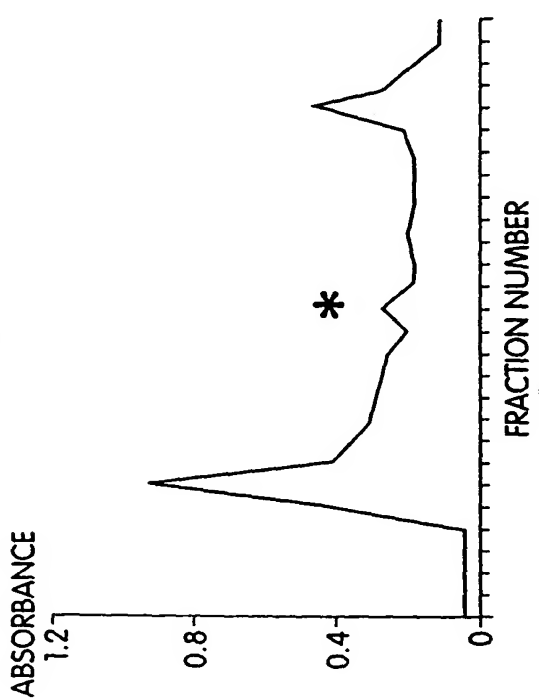


Fig. 10C

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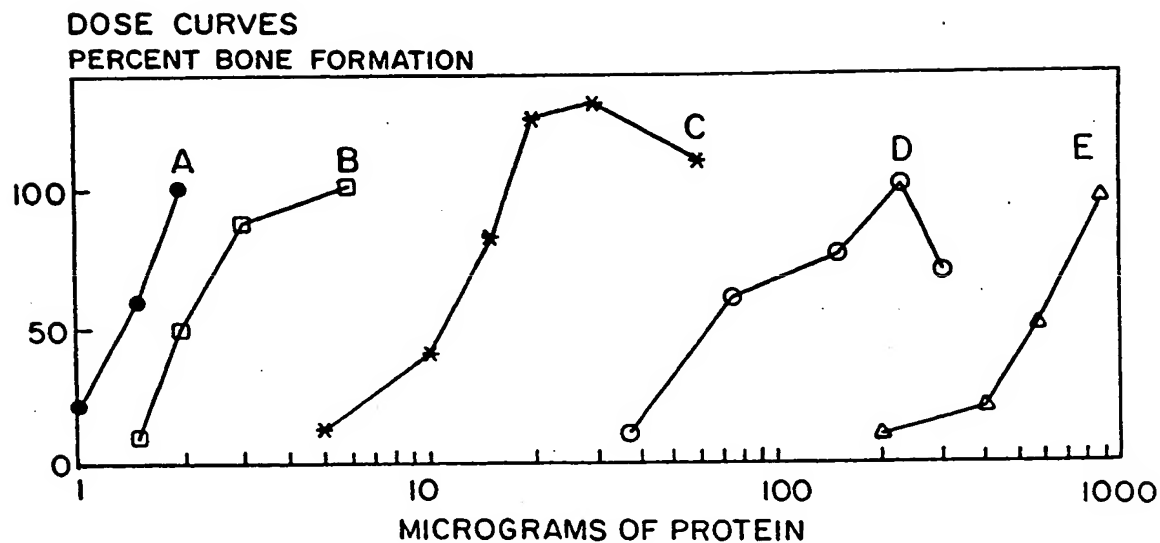


Fig. 11

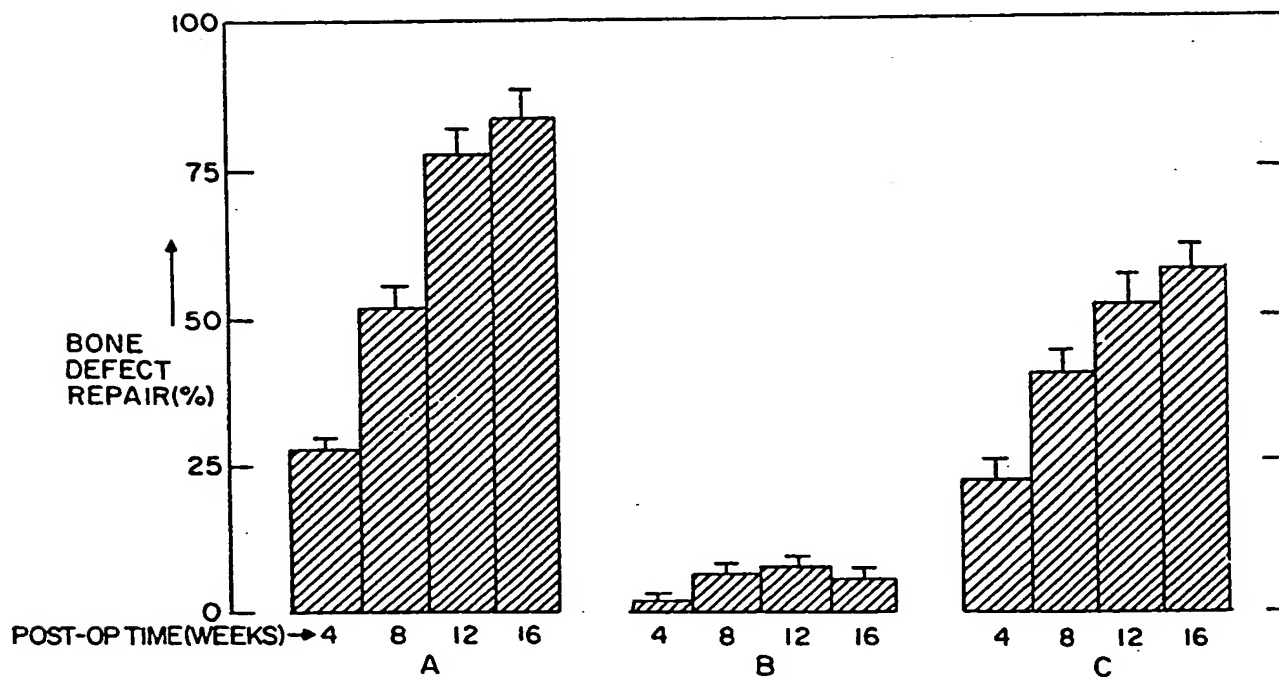


Fig. 12

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```

      10      20      30      40      50
GATCCTAATGGGCTGTACGTGGACTTCCAGCGCGACGTGGGCTGGGACGA
D P N G L Y V D F Q R D V G W D D

      60      70      80      90     100
CTGGATCATCGCCCCGTCGACTTCGACGCCTACTACTGCTCCGGAGCCT
W I I A P V D F D A Y Y C S G A

      110     120     130     140     150
GCCAGTTCCTCTGCGGATCAATTCAACAGCACCAACCACGCCGTGGTG
C Q F P S A D H F N S T N H A V V

      160     170     180     190     200
CAGACCCTGGTGAACAACATGAACCCCGGCAAGGTACCCAAGCCCTGCTG
Q T L V N N M N P G K V P K P C C

      210     220     230     240     250
CGTGCCCAACGAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATT
V P T E L S A I S M L Y L D E N

      260     270     280     290     300
CCACCGTGGTGCTGAAGAACTACCAGGAGATGACCGTGGTGGGCTGCGGC
S T V V L K N Y Q E M T V V G C G

      310
TGCCGCTAACTGCAG
C R *
```

Fig. 13

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SDS GEL ELUTION OF OSTEOGENIC ACTIVITY

CALCIUM CONTENT (ug/mg tissue)

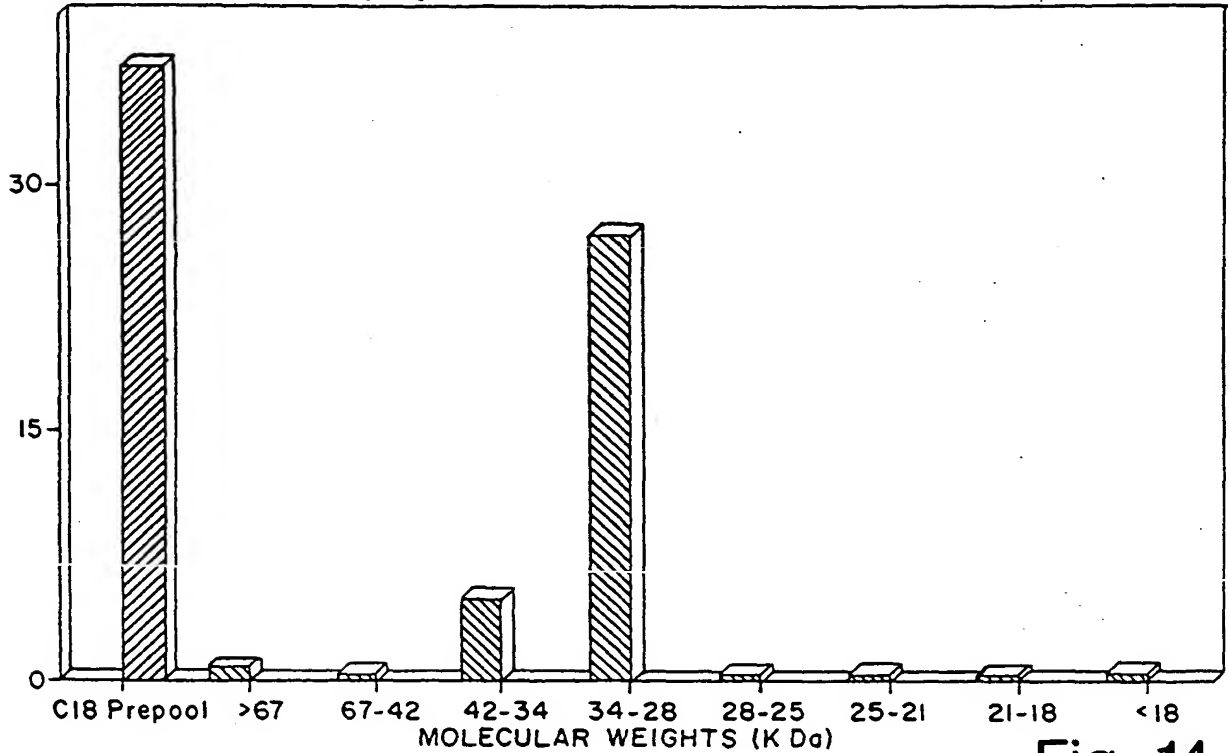
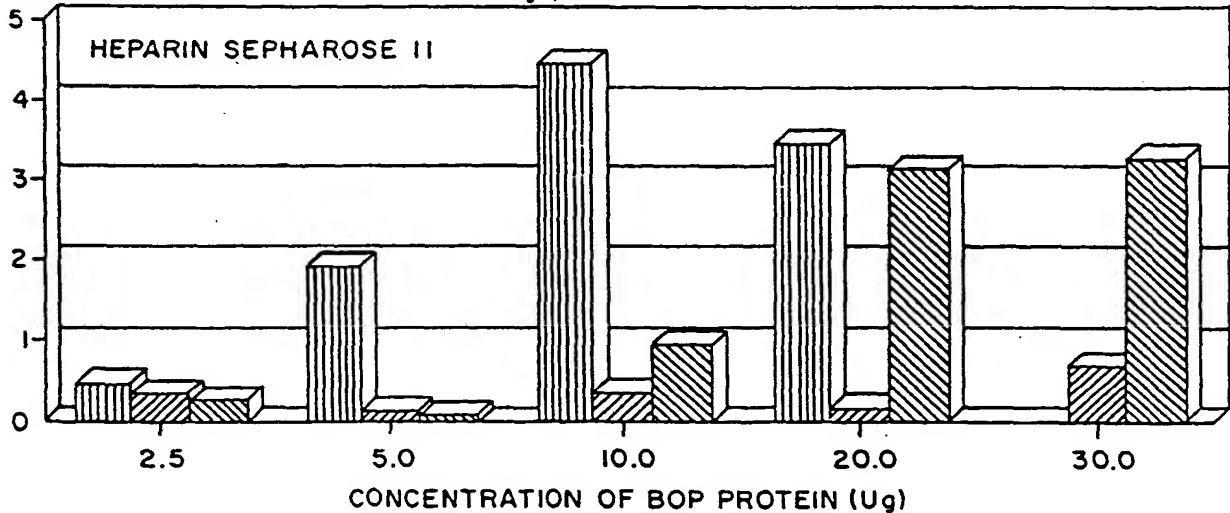


Fig. 14

ALKALINE PHOSPHATASE (U/mg protein)



||||| RAT MATRIX

////// BOVINE MATRIX

\\\\\\\\ DEGLY. BOVINE MATRIX

Fig. 19

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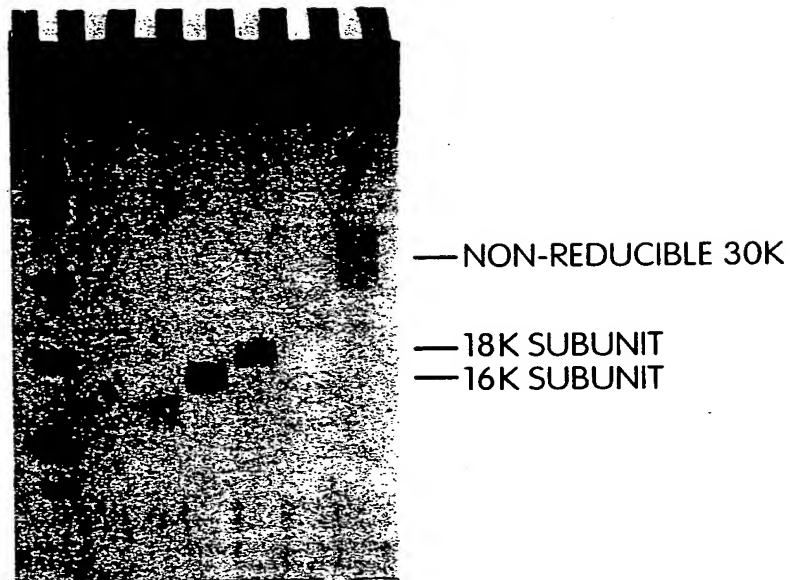


Fig. 15

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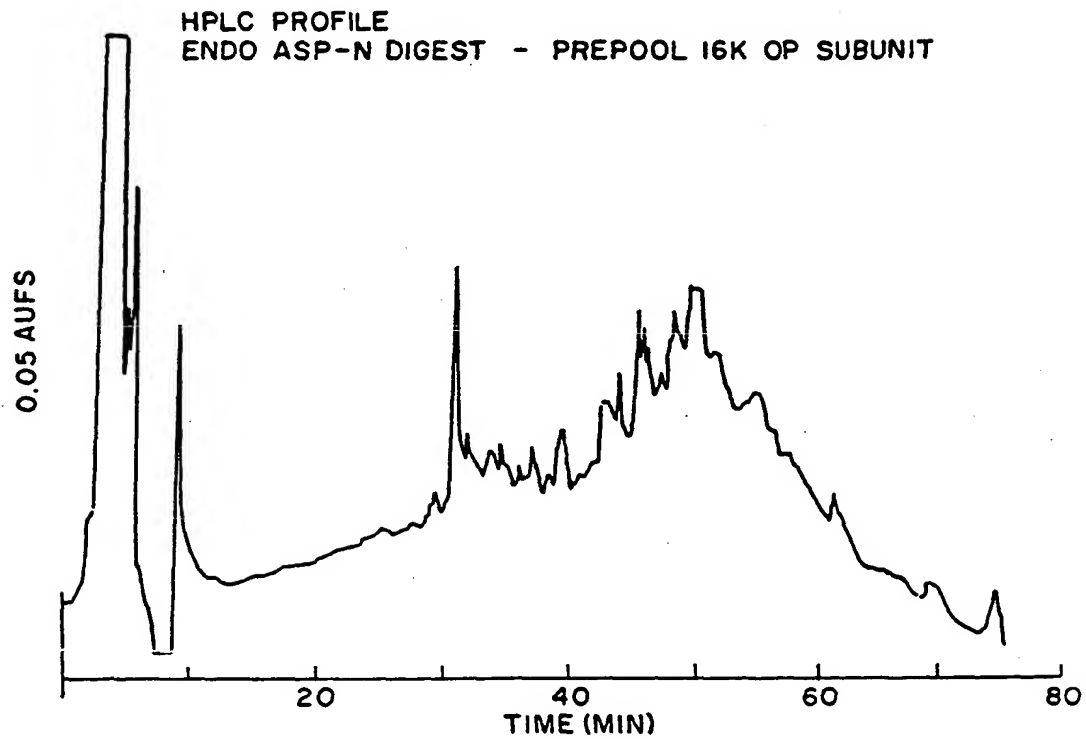


Fig. 16A

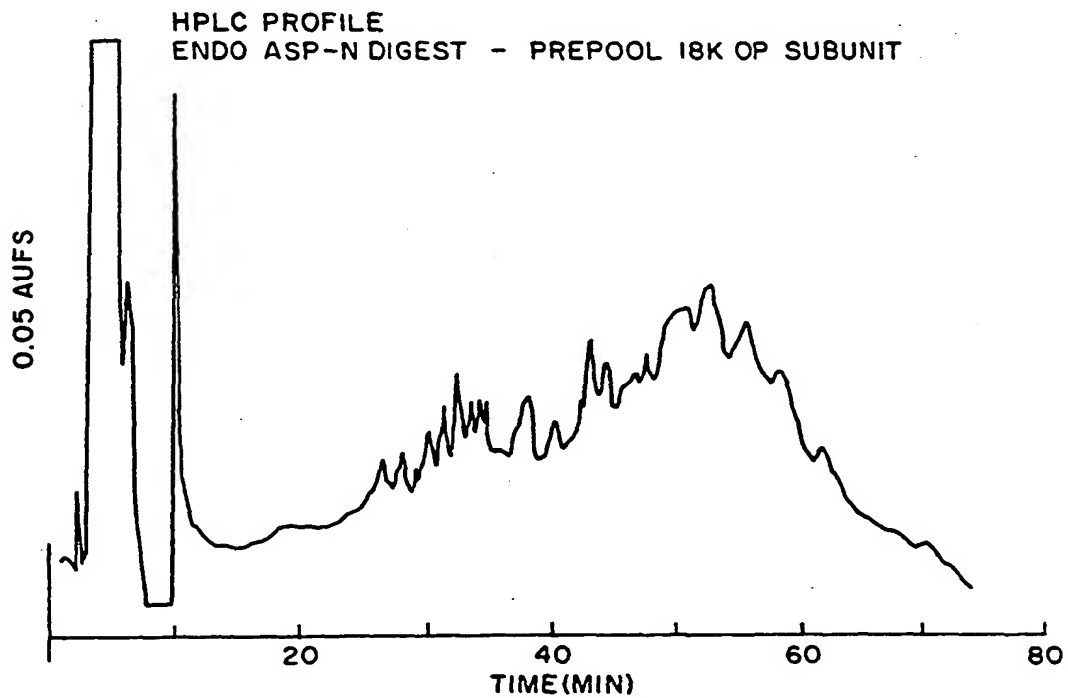


Fig. 16B



Fig. 17A

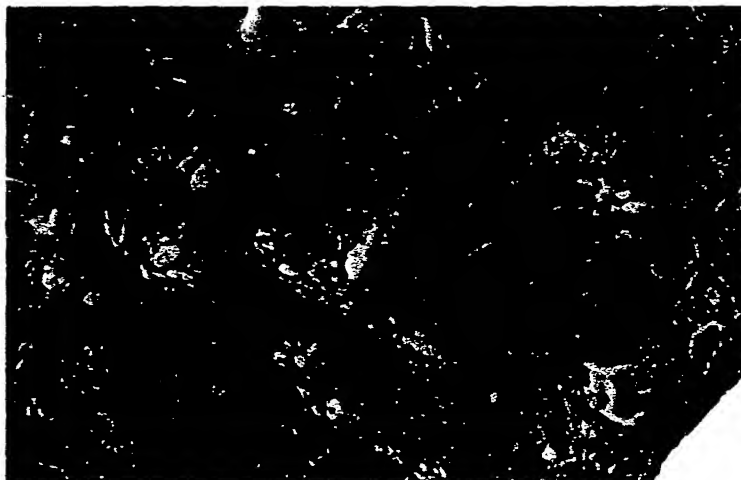


Fig. 17B



Fig. 17C

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		:VGL DPP OP1 CBMP2 :CBMP3 beta--		TGF- :MIS alpha::		consensus	
		a) b):(bov)Inhibin		beta : Inhib::		choices	
COP1	COP5	COP3	COP4	1 2 3:			
<P	P	C	C	C	C	C	C
N	N	K	K	C	H	R	k,r
G	G	R	R	V	R	V	k,r
L	L	H	H	L	A	L	h,k,r,q
Y	Y	S	S	V	E	V	p,s,e,q
V	V	L	L	P	L	P	l
D	D	Y	Y	P	S	S	y,f
F	F	V	V	I	N	I	v,i
F	F	E	E	D	S	S	d,e,s
Q	Q	F	F	F	I	I	f
R	R	D	D	R	S	S	k,r,s
D	D	F	F	K	Q	Q	d
V	V	A	A	R	A	A	v,l,i
G	G	D	D	Q	E	E	g
W	W	I	I	:	L	L	w
D	D	S	S	:	G	G	q,n,d,e,s
D	D	E	E	:	W	W	d,e,n
W	W	W	W	:	E	E	w
I	I	I	I	:	R	R	i,v
I	I	S	S	:	W	W	i,v
A	A	P	P	:	I	I	a,s
P	P	K	K	:	V	V	p
P	P	S	S	:	Y	Y	e,q,p*
G	G	F	F	:	P	P	g,s
Y	Y	D	D	:	S	S	y,f
H	H	A	A	:	F	F	h,d,n,q,y*
A	A	A	A	:	I	I	a
A	A	A	A	:	F	F	

Fig. 18-1

Fig. 18-2

Fig. 18-3

Fig. 18-4

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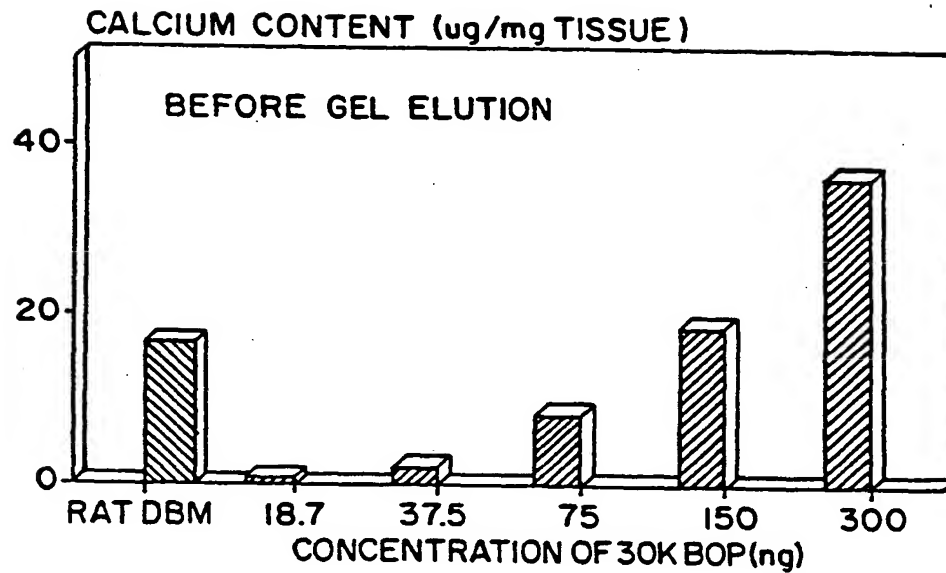


Fig. 20A

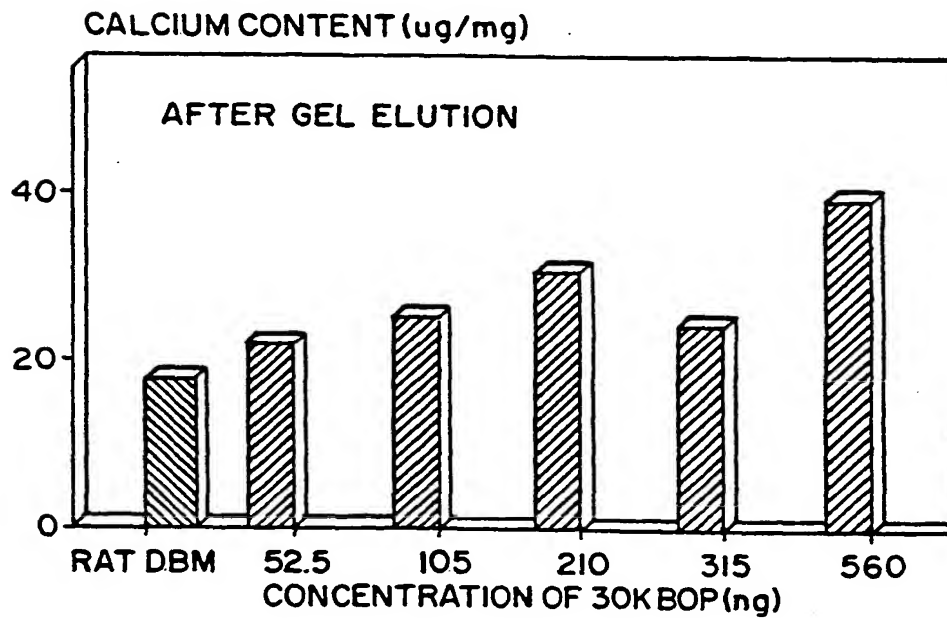


Fig. 20B

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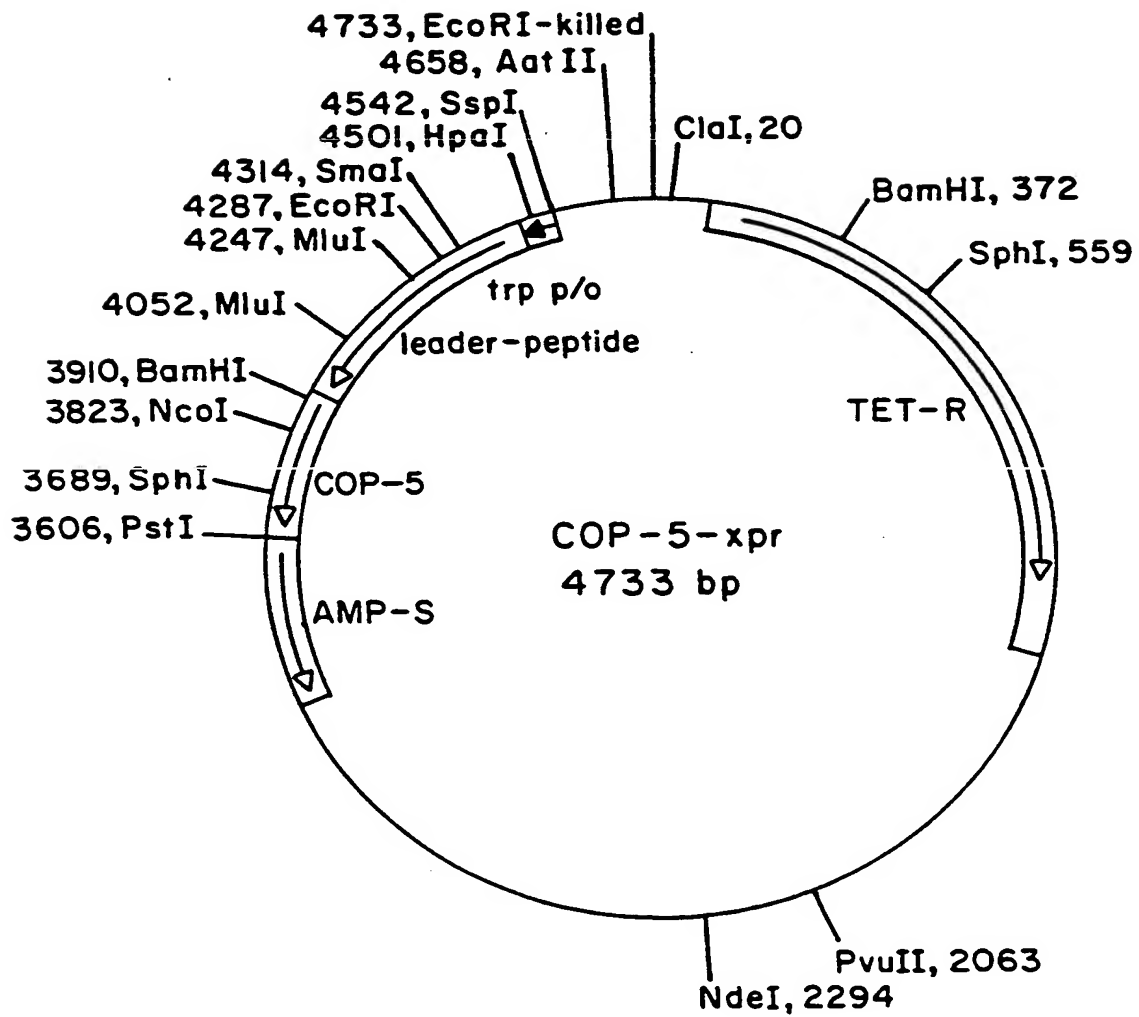


Fig. 21A

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COP-5 fusion protein

```

      10      20      30      40      50
ATGAAAGCAATTTTCGTA CTGAAAGGTTCACTGGACAGAGATCTGGACTC
M K A I F V L K G S L D R D L D S
                               BglII

      60      70      80      90     100
TCGTCTGGATCTGGACGTTCTG TACCGACCACAAAGACCTGTCTGATCACC
R L D L D V R T D H K D L S D H

     110     120     130     140     150
TGGTTCTGGTCGACCTGGCTCGT AACGACCTGGCTCGTATCGTTACTCCC
L V L V D L A R N D L A R I V T P
          SalI                               Sma

     160     170     180     190     200
GGGTCTCGTTACGTTGCGGATCTGGAATTCATGGCTGACAACAAATTCAA
G S R Y V A D L E F M A D N K F N
I                               EcoRI

     210     220     230     240     250
CAAGGAACAGCAGAACGCGTTCTACGAGATCTTGACACCTGCCGAACCTGA
K E Q Q N A F Y E I L H L P N L
          MluI           BglII       BspMI+

     260     270     280     290     300
ACGAAGAGCAGCGTAACGGCTTCATCCAAAGCTTGAAGGATGAGCCCTCT
N E E Q R N G F I Q S L K D E P S
                               HindIII

     310     320     330     340     350
CAGTCTGCGAATCTGCTAGCGGATGCCAAGAACTGAACGATGCGCAGGC
Q S A N L L A D A K K L N D A Q A
          NheI                               FspI

     360     370     380     390     400
ACCGAAATCGGATCAGGGGCAATTCATGGCTGACAACAAATTCAACAAGG
P K S D Q G Q F M A D N K F N K

     410     420     430     440     450
AACAGCAGAACGCGTTCTACGAGATCTTGACACCTGCCGAACCTGAACGAA
E Q Q N A F Y E I L H L P N L N E
          MluI           BglII       BspMI+

     460     470     480     490     500
GAGCAGCGTAACGGCTTCATCCAAAGCTTGAAGGATGAGCCCTCTCAGTC
E Q R N G F I Q S L K D E P S Q S
                               HindIII

```

Fig. 21B-1

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510 520 530 540 550
TGCGAATCTGCTAGCGGATGCCAAGAACTGAACGATGCGCAGGCACCGA
A N L L A D A K K L N D A Q A P
NheI FspI

560 570 580 590 600
AGGATCCTAATGGGCTGTACGTCGACTTCAGCGACGTGGGCTGGGACGAC
K D P N G L Y V D F S D V G W D D
BamHI SalI

610 620 630 640 650
TGGATTGTGGCCCCACCAGGCTACCAGGCCTTCTACTGCCATGGCGAATG
W I V A P P G Y Q A F Y C H G E C
StuI NcoI BsmI+

660 670 680 690 700
CCCTTTCCCGCTAGCGGATCACTTCAACAGCACCAACCACGCCGTGGTGC
P F P L A D H F N S T N H A V V
NheI DraIII
PflMI

710 720 730 740 750
AGACCCTGGTGAACCTCTGTCAACTCCAAGATCCCTAAGGCTTGCTGCGTG
Q T L V N S V N S K I P K A C C V
MSTII

760 770 780 790 800
CCCACCGAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATGAGAA
P T E L S A I S M L Y L D E N E K
SphI

810 820 830 840 850
GGTGGTGCTGAAGAACTACCAGGAGATGGTAGTAGAGGGCTGCGGCTGCC
V V L K N Y Q E M V V E G C G C
PflMI

860
GCTAACTGCAG
R *
PstI

Fig. 21B-2

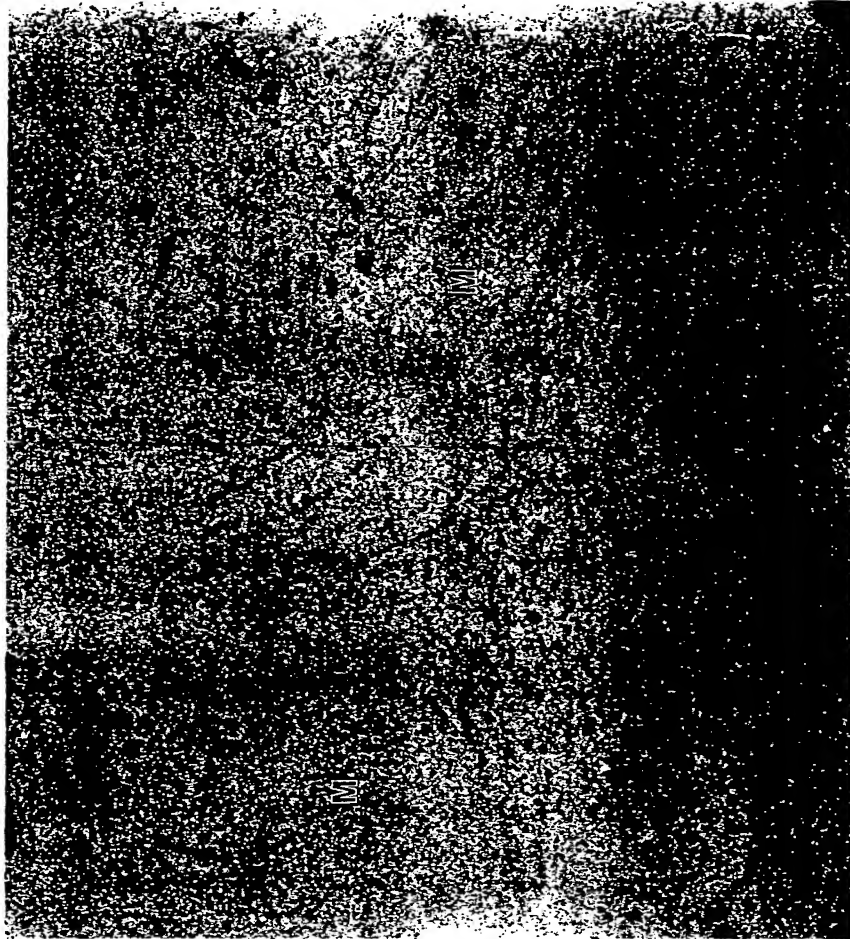


Fig. 22A

30/30



Fig. 22B